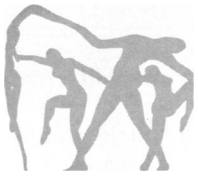

Women and Medicine

A Woman's Heart
An Update of Coronary Artery Disease Risk in Women

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Coronary artery disease accounts for a third of all deaths in women. Traditionally, studies on this disease have been conducted with male subjects. A growing body of evidence indicates that oral contraceptive and postmenopausal estrogen use present risk factors for the disease that are unique to women. In addition, sex differences exist with regard to the relationship of most of these risk factors to the development of the disease. An understanding of these differences has an important role in expanding the management of coronary artery disease risk reduction for women and in defining directions for future research.

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Coronary artery disease is well recognized as the leading cause of death in men. Although women have been considered to be protected from the disease, they are not immune from it.[1] Each year nearly 250,000 women in the United States die of events related to coronary artery disease, including cerebrovascular accidents.[2] This accounts for a third of all female deaths.

Despite the rise in the death rate from heart disease as a woman ages, 200,000 such deaths occur prematurely (before the age of 65 years).[3] This statistic emphasizes the importance of the disease in women as a major issue in preventive cardiology. The goal of preventive care is to postpone the occurrence of chronic disease events. Therefore, it appears that a considerable amount of mortality and morbidity could be reduced in the female population by preventive intervention involving modifiable risk factors.

Whether preventive cardiology measures can reduce the incidence of coronary artery disease in women is not clearly established for all recognized risk factors. Most of the scientific research involving prevention of the disease has been done in male subjects. Because men represent the high-risk sex with respect to coronary artery disease, in consideration of cost- and time-effectiveness, the study of the disease has generally been restricted to men.

Uncertainty exists whether research regarding coronary artery disease can be extrapolated from men to women. Most of the recommendations for risk intervention in women, however, have been based on studies involving male subjects. Despite these uncertainties, population trends of coronary artery disease events in women suggest that its risk can be modified in the female population. Since 1963, women in this country have experienced a 43% drop in deaths from both myocardial infarction and cerebrovascular accident.[3] Most of this decline has occurred since 1972. These trends in the incidence of heart disease may reflect the contemporary reductions in saturated fat intake and cigarette smoking that occurred in our population during this period.[4]

In general, the relationship of coronary artery disease events to risk factors in women appears to be similar to that in their male counterparts with respect to major modifiable risk factors such as high plasma cholesterol levels, cigarette smoking, and hypertension. The role, however, of other coronary artery disease risk factors such as diabetes mellitus, the use of estrogen hormones, physical activity, personality and stress, obesity, and even pregnancy in promoting the disease may be different and unique for women. The purpose of this article is to review the current knowledge of the risk of coronary artery disease as it relates to women. The current explanations for the male-female difference in that risk will be considered, as will the role of the individual risk factors in women. An understanding of these differences has an important role in expanding the management of risk reduction for women and defining directions of future research.

Female Protection

The process of atherosclerosis begins in childhood. The period of life when sex differences in coronary artery disease risk occur is uncertain. The difference in the incidence of myocardial infarction between adult men and women corresponds to differences noted in the extent of atherosclerosis at autopsy. A comparison of the percent of aortic surface involvement by atherosclerotic lesions from autopsy findings indicates that men have approximately 50% more atherosclerosis than women.[5]

The sex difference in the disease incidence has been attributed to "female protection." Included under this nebulous umbrella are both male-female psychosocial and biologic differences.[6] Biologic factors, in particular gynecoid hormones, appear to have a major role in promoting female protection.[7] Plasma lipid and lipoprotein levels bear impor-

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ABBREVIATIONS USED IN TEXT

HDL = high-density lipoprotein
LDL = low-density lipoprotein
MRFIT = Multiple Risk Factor Intervention Trial
NCEP = National Cholesterol Education Program
VLDL = very-low-density lipoprotein

tant relationships to coronary artery disease risk that will be considered in more detail later. Female protection appears to be mediated by hormonally induced changes in plasma lipids and lipoproteins. Specifically, estrogen appears to confer female protection through its role in promoting increases in the cardioprotective high-density lipoprotein (HDL) cholesterol. Two lines of evidence support this explanation. Population studies indicate that sexual maturation is associated with a sex-related divergence in plasma lipoprotein profiles.[8,9] At puberty, levels of low-density lipoprotein (LDL) cholesterol and HDL cholesterol decrease in both boys and girls, but the decrease in HDL cholesterol is much greater in the boys.

Second, estrogen administration has been shown to promote increases in HDL cholesterol.[10-13] The interpretation of the pharmacologic effects of estrogens on plasma lipids and lipoproteins may be different from physiologic effects. While the precise mechanism of female protection needs to be more clearly defined, it appears that the biologic effects of estrogen on plasma lipids and lipoproteins represent an important aspect of female protection. In addition, there may be male-female psychosocial differences that affect the atherosclerotic process and susceptibility for coronary artery disease.

Plasma Lipids and Lipoproteins

Elevated plasma cholesterol levels are a well-established risk factor for coronary artery disease. Studies in male subjects with hypercholesterolemia—a cholesterol level greater than 6.76 mmol per liter (260 mg per dl)—indicate that reductions in the plasma cholesterol level reduce coronary artery disease events.[14,15] Whether reducing plasma cholesterol levels in women lowers heart disease risk has not been directly shown. The Framingham study, however, has shown that elevated plasma cholesterol values are related to an increased incidence of coronary artery disease events in women younger than 50 years.[16] In this population, while plasma HDL-cholesterol levels were higher in the women than in the men, HDL cholesterol remained the strongest lipid predictor of coronary artery disease in both sexes.[17] The ratio of the total cholesterol level to the HDL cholesterol has been developed to enhance the heart disease predictive capability of these two measurements. Increasing total cholesterol to HDL-cholesterol ratios are predictive of an increasing rate of such events in women aged 60 to 69 years.[17]

Hypertriglyceridemia as a risk factor for coronary artery disease has long been a controversial issue.[18] Multivariate analysis techniques in male subjects have been unable to show a significant relationship between plasma triglyceride levels and disease events. This has been attributed to triglyceride interaction with more powerful risk factors. In particular, the low levels of plasma HDL cholesterol that generally occur concomitantly with hypertriglyceridemia may reduce the strength of the relationship of plasma triglyceride values to disease risk by multivariate analysis. Data from the Framingham study, however, indicate that for women, but not for men, hypertriglyceridemia appears to be an independent coronary artery disease risk factor on multivariate analysis.[17,19]

While women enjoy more favorable lipoprotein profiles than men, a beneficial reduction in plasma cholesterol levels is indicated for women with high-risk levels. The National Cholesterol Education Program (NCEP) recently established definite high-risk values for total plasma cholesterol as 6.24 mmol per liter (240 mg per dl) and a desirable plasma cholesterol level below 5.20 mmol per liter (200 mg per dl).[20] Therapeutic intervention strategies for the management of lipid disorders (beyond the scope of this article) are presented in the NCEP panel's report.[20] While these recommendations are based primarily on studies of male subjects and may appear to be directed towards men, they were meant to be applied to both women and men.

Cigarette Smoking

The relationship of cigarette smoking to coronary artery disease risk is well established.[21,22] The Nurses' Health Study showed a greater than fivefold increase in fatal myocardial infarction events in women smokers compared with nonsmokers who were followed prospectively over a six-year period.[23] Conversely, the cessation of cigarette smoking by women smokers returns their risk of myocardial infarction to that of women who never smoked.[24] Despite the decrease in cigarette smoking since the Surgeon General's antismoking statement in 1964, this reduction has favored men.

Although women smokers tend to smoke fewer cigarettes than men smokers, recent smoking trends indicate that since 1980 younger women—aged 20 to 24 years—appear to be increasing their cigarette consumption, both in terms of the total number of women smoking and the number of cigarettes smoked per person.[25] This finding is especially disconcerting because women in this age bracket tend also to be users of oral contraceptives. After accounting for age, the risk for myocardial infarction in oral contraceptive users who smoke more than 25 cigarettes a day is almost eightfold above that in nonsmoking oral contraceptive users and 40 times greater than the risk for nonsmoking women not using oral contraceptives.[26] This risk is even higher with increasing age. Clearly more effort is needed to prevent smoking in young women, who are currently being targeted by the tobacco industry.

Blood Pressure

The trends in blood pressure management over the past decades reflect the medical care system's recognition of elevated blood pressure as a risk factor for coronary artery disease. Since the early 1960s, mean systolic blood pressures have dropped from 129 to 123 mm of mercury among white and 138 to 123 mm of mercury among black women of ages 25 to 74 years.[27] In addition, there has been a significant decline in the prevalence of definite high blood pressure—systolic pressure, 160 mm of mercury or higher; diastolic pressure, 95 mm of mercury or higher—for both groups since the early 1970s after adjusting for aging. This has been related to increased therapeutic intervention in blood pressure management, as there has been an increase in the percentage of women diagnosed with hypertension, receiving antihypertensive medications, and whose hypertension was controlled with medication during this time period.

Evidence from the Framingham study has indicated an increase in successful hypertensive treatment since 1960.[28]

Associated with successful treatment was a significant decline in coronary artery disease events in treated women compared with untreated hypertensive women. This difference was particularly pronounced for women whose previous systolic blood pressures were above 180 mm of mercury.

Although the importance of the relationship of isolated systolic pressures to coronary artery disease risk has been controversial, the Framingham data indicate that the prevalence of isolated systolic hypertension, which increases in both sexes after the age of 55 years, is greater in women.[29] In this study, an elevated isolated systolic blood pressure was predictive of coronary artery disease for women older than 55 years.

An interesting facet of sex differences in the relationship of hypertension to heart disease risk is that the prognosis of essential hypertension (when comparisons are made between groups with equivalent age and severity of disease) is better for women than for men.[30] This finding has been attributed to the presence of more severe atherosclerotic disease concomitant with hypertension in the men, which could aggravate the effects of hypertension on the disease.

More recently there are data that indicate that the hemodynamic events which occur in persons with hypertension when subjected to isometric exercise stress testing are different for men and women.[31] Isometric handgrip exercise in 100 women with hypertension matched to 100 men by mean arterial pressure, age, race, and body surface area induced a significantly greater mean arterial pressure and total peripheral vascular resistance in the men compared with the women subjects. These findings are consistent with other reports that estrogen therapy in women can reduce blood pressure[32] and that women with higher blood estrogen levels experienced less increase in arterial blood pressure when experimentally subjected to increasing mental stress.[33] These findings may be particularly relevant in explaining sex differences that are noted with respect to coronary artery disease and psychosocial stress. Perhaps reactivity in hemodynamic responses to physical and emotional stress is more critical to disease prognosis than is the resting blood pressure value.

A particular issue of blood pressure and women involves the use of oral contraceptives containing progestinal agents in addition to estrogen. Cross-sectional data indicate that oral contraceptive use is associated with a 2.7 times higher incidence of hypertension compared with that in women not using oral contraceptives. A 5- to 6-mm-of-mercury greater systolic pressure and 1- to 2-mm-of-mercury greater diastolic pressure persisted in the oral contraceptive users who continued to use the pills on follow-up examinations.[34] An increase of more than 10 mm of mercury in the systolic pressure and of almost 10 mm of mercury in the diastolic pressure has been reported with the use of oral contraceptives over a three-year period.[35] The blood pressure generally returned to pretreatment levels within three months of stopping the use of oral contraceptive medication.

The importance of treating hypertension is well established. Current therapeutic regimens are being reassessed, however, in view of reported unfavorable effects of certain antihypertensive medications on plasma lipids and lipoproteins.[36] Although this issue is currently under critical appraisal, it would seem prudent not to defer medical management of a patient with definite hypertension because of these concerns. Selecting antihypertensive medications with the least lipid-altering effects is a sensible approach.

Diabetes Mellitus

The presence of diabetes mellitus is an important risk factor for women older than 45 years.[21,37] Persons with diabetes appear to have a twofold increase in coronary artery disease risk compared with those without diabetes, adjusting for age, systolic blood pressure, cigarette smoking, total cholesterol levels, and left ventricular hypertrophy.[38] Because the incidence of diabetes mellitus is greater among women than among men, this risk factor is of considerable importance for women.[2,38,39] In addition, the death rate from myocardial infarction for diabetic women exceeds that for diabetic men.[37] Another concern for the female population is the increase in reported incidence of diabetes mellitus in women since the early 1960s.[40] These findings emphasize the importance of the early recognition of diabetes mellitus, particularly for women.

Overweight

Defining obesity as being equal to or greater than the 85th percentile of the body mass index—weight in kilograms divided by height in meters squared—of 20- to 29-year-old men and women, 24% of women (compared with 14% of men) between the ages of 18 and 74 years are obese.[41] The role of obesity and overweight has long been recognized for its deleterious influence on other coronary artery disease risk factors such as diabetes mellitus and low plasma HDL-cholesterol levels, which represent confounding variables in interpreting obesity and heart disease risk.[42,43] The relative weight expressed as a percentage of desirable weight was shown to be an independent risk factor in a cohort of 2,818 women over a 26-year period.[44] The percent body fat has been shown to increase with age from 20% in 18-year-old women to 30% to 40% during adult life. Likewise, the incidence of obesity increases by almost threefold during this period until leveling off around the age of 65 years.[45] Trends in the incidence of obesity in women are somewhat encouraging. While 25.1% of women aged 20 to 74 years were defined as obese in 1960, the incidence had dropped to 23.8% by 1974.[41] The socioeconomic status appears to have a substantial impact on obesity, as excess body weight is reported to be up to 12 times more frequent in women of lower socioeconomic than of high socioeconomic classes.[46] A continued emphasis on reducing body fat in overweight women is needed in addition to the development of appropriate weight standards and tools that conveniently measure body fat.

An interesting note is differences between female (gynecoid) and male (android) fat distributions expressed by the ratio of the waist to hip circumference with respect to the coronary artery disease risk in women.[47] The waist/hip ratio measured in 1,462 women was more strongly associated with coronary artery disease events over a 12-year period than were indices of obesity (body mass index and sum of skin-fold measurements). The relationship of the waist/hip ratio to disease events persisted with multivariate analysis of traditional coronary artery disease risk factors.[47] The android (high waist/hip circumference ratio) distribution is associated with higher incidences of coronary artery disease than the gynecoid (low waist/hip circumference ratio) distri-

bution in both men and women.[48,49] These findings may be useful to clinicians for identifying heart disease risk.

Exogenous Hormones

Although biologic levels of female hormones appear to exert a protective effect, the role of exogenous hormones on coronary artery disease risk is being defined. These exogenous hormones include both oral contraceptives and postmenopausal estrogen replacement. The declining prevalence in the use of oral contraceptives in women of all age groups between 1970 and 1980 mainly reflects a decreased use among married women because increased use is reported among single and never-married women.[50,51]

The effects of oral contraceptives on plasma lipid levels represent the combined effects of the hormonal constituents, estrogen and progestins. Early reports indicated that oral contraceptives containing high doses of estrogen caused an increased incidence of myocardial infarction,[52-55] which is particularly increased by concurrent cigarette smoking.[26,52,54,55] Because of the often disparate biologic effects of estrogen and progesterone, it is important to consider the relationship of oral contraceptive use to coronary artery disease risk factors in terms of the individual estrogen and progestin components. Estrogen appears to raise plasma triglyceride and HDL-cholesterol levels, and progestinal agents lower the HDL cholesterol.[11-13] An additional risk potentiation from oral contraceptive use, which may contribute to atherogenesis, is an increased ratio of very-low-density lipoprotein (VLDL) cholesterol to VLDL triglyceride that occurs with the use of progestin-predominant pills.[12] The newer low-dose oral contraceptives (lower estrogen) appear to have a neutral effect on HDL-cholesterol levels.[13] Oral contraceptive use can also increase plasma triglycerides and blood pressure[35,56] and aggravate diabetes mellitus.

Estrogens are commonly taken after the menopause to reduce menopause-related symptoms. The relationship of this practice to the risk of coronary artery disease is unclear. The postmenopausal use of conjugated and esterified estrogens is associated with increased levels of plasma HDL cholesterol.[11] Because biologic levels of estrogen are associated with premenopausal risk reduction, it would seem that estrogen replacement for postmenopausal women would have a role in reducing risk. This notion is supported by findings that among women with surgically induced menopause (bilateral oophorectomy), a greater relative risk of a subsequent myocardial infarction was noted for the women who had had an operation at younger ages.[57] In a similar line of evidence, a comparison of the incidence of coronary artery disease in a group of women younger than 35 years at the time of either bilateral or unilateral ovariectomy revealed a disease incidence of 25% in the bilateral ovariectomy group versus a 3% incidence in the unilateral ovariectomy group over the ensuing 20 years.[58]

Data from case-control studies on the relationship of the risk of myocardial infarction in women using postmenopausal estrogen are conflicting.[59-62] Evidence from the Lipid Research Clinics study supports a coronary artery disease risk reduction associated with postmenopausal estrogen use.[63] This study noted a third lower relative incidence of myocardial infarction deaths with estrogen use compared with nonuse in women aged 40 to 69 years over an 8.5-year period after adjusting for potential confounding factors.[63] This contrasts with an earlier report from the Framingham study that indicated a doubled incidence of myocardial infarction and of cerebrovascular accident among estrogen users compared with nonusing counterparts.[64] When the Framingham study data were adjusted for smoking, however, the risk for myocardial infarction disappeared but the risk for cerebrovascular accident persisted.[65] An important aspect in interpreting these disparate findings involves issues of the type and dose of estrogen used and the duration of estrogen therapy.

On the other hand, estrogen supplementation in men does not decrease the incidence of coronary artery disease compared with placebo and may actually increase the incidence of adverse medical effects.[66] More study is indicated to clarify the role of postmenopausal estrogen use in women because the effects of estrogen replacement may be related to the type of estrogen given and also to the timing of replacement with respect to the start of menopause.

Physical Activity

Physical inactivity is recognized as a coronary artery disease risk factor in men.[67] The Harvard alumni study has established that men who expend greater than 2,000 calories a week through leisure-time physical activity have a reduced incidence of heart disease events when compared with sedentary—less than 500 calories a week—counterparts.[68] These findings are confirmed by a recent publication of the Multiple Risk Factor Intervention Trial (MRFIT).[69] Whether these findings apply to women has not been clearly established.

Current exercise training recommendations formulated by the American College of Sports Medicine are based on exercise regimens designed to increase maximal aerobic work capacity ("The Recommended Quantity and Quality of Exercise for Developing and Maintaining Fitness in Healthy Adults," American College of Sports Medicine position statement, 1987). With respect to coronary artery disease risk factor modifications, exercise training studies in men indicate that aerobic exercise training has favorable effects on plasma lipoproteins by raising the HDL-cholesterol level.[70] Regular exercise also may reduce the blood pressure and control body weight. In contrast to studies in men, exercise training studies in women have not uniformly shown an increase in HDL-cholesterol levels in women either before or after the menopause.[71-74] The reason for this difference in sex responses to exercise training with respect to HDL-cholesterol levels is unclear but has been attributed to intrinsically higher HDL-cholesterol levels in women. Greater exercise training-induced increases in HDL cholesterol are shown in women with low preexercise training HDL-cholesterol levels than in women with higher pretrained values.

A current issue in the areas of exercise and health promotion is findings that suggest that the sort of physical activity needed to lower heart disease risk may be of lower work intensity than what is currently recommended. The MRFIT study indicated that despite a reduction in coronary artery disease events in men who were more physically active based on leisure-time activities, less than 5% of the total group achieved the intensity of physical work currently recommended for exercise training.[69]

Although comparable studies with respect to leisure-time physical activity and heart disease have not been done in women, the relationship of physical activity to coronary risk factors in postmenopausal women indicates that physical ac-

tivity as measured by the Paffenbarger index is significantly related to increasing HDL_3 cholesterol but not HDL cholesterol or HDL_2 cholesterol.[75] On the other hand, when the sports activity index component of a questionnaire was used, a significant positive correlation was found between increasing sports activity and HDL cholesterol and the HDL_2-cholesterol but not the HDL_3-cholesterol subfraction. This indication that higher work intensity levels may be necessary in women to effect increases in HDL cholesterol is supported by a significant positive correlation between maximal aerobic work capacity and HDL-cholesterol levels in a group of 3,900 healthy women aged 18 to 61 years.[76] Likewise, total reported energy expended in leisure-time physical activity was not significantly related to HDL-cholesterol levels in women sampled in the Minnesota heart survey, whereas heavy-intensity work—6.0 kcal per minute or more—was significantly correlated with increasing HDL-cholesterol levels.[77] In contrast, significant positive correlations were found between both activity scores and HDL-cholesterol levels in men. Further study is indicated to delineate the effects of both physical activity and exercise training in men and women with respect to the mechanisms of coronary artery disease risk reduction (including plasma lipids and lipoproteins, blood pressure, obesity, fibrinolysis, and platelet adhesion).[78]

Psychosocial and Personality

Psychosocial differences may play an important role in affecting sex differences in heart disease risk. Male-female differences in health practices that are related to coronary artery disease have also been shown to be possibly related to psychosocial differences.[79] Among 3,516 men and women aged 30 to 69 years, a higher percentage of men than women smoked cigarettes.

The notion of "stress" has been widely popularized by the lay press as causative of coronary artery disease. The terminology in the area of stress and psychosocial behavior, once somewhat nebulous, is being more clearly defined. While doubt has been recently cast on the relationship of type A behavior with heart disease risk,[80] a cautious interpretation of this study is quick to point out that it is likely that certain components of the type A personality, rather than type A behavior as a whole, are related to the risk.[81] The type A behavior pattern, which represents a cluster of behavior traits, including hostility, aggressiveness and anger that are strongly suppressed, tenseness, hyperalertness, explosive speech style, impatience, and a continuous sense of time urgency, has been shown to be positively related to the risk of coronary artery disease in women.[21,82,83]

In the Framingham study, employed persons of both sexes tended to have a higher incidence of type A behavior than did their nonemployed counterparts. The incidence of type A behavior was most prevalent in older employed women and younger housewife subgroups.[82] For both women with jobs and housewives, however, type A behavior did represent an increased risk for coronary artery disease. While employed women tend to show more type A characteristics than their unemployed counterparts, this tendency is particularly prevalent between the ages of 30 and 35 years.[84] The peak in type A scores in employed women between the ages of 30 and 35 years is not noted in men and is attributed to the belief that type A women are less likely to leave their jobs when they have children. The Framingham study has shown type A behavior to be related to psychosocial states that may explain the relationship of this behavior pattern to disease risk: daily stress, emotional lability, tension, anger symptoms, and ambition.[85] The prevalence of these psychosocial factors appeared to diminish with age. Examination of the relationship of the prevalence of these factors to employment indicates a similar prevalence of psychosocial factors between employed women and men, but not between employed women and housewives.

Women with jobs—including both white- and blue-collar—were subclassified as clerical or nonclerical workers. Clerical workers were found to have an increased incidence of coronary artery disease.[86] In addition, the incidence of the disease in women increased with an increasing number of children. The incidence of disease was highest for clerical women whose husbands had blue-collar jobs. These findings suggest that the excessive risk in clerical workers with husbands in blue-collar jobs and children may be related to the stresses of economic pressures coupled with low job mobility.[82]

Sex differences in coronary artery disease risk as they relate to personality and psychosocial factors are also present in a study of cynomolgus macaques. A dominant social status in female monkeys is associated with less atherosclerosis than is noted in either dominant or subordinate male macaques and subordinate females.[87,88] Compared with subordinate females, the dominant group had regular ovarian function and relatively smaller adrenal glands, indicating they experienced less social stress. Because levels of plasma lipids and lipoproteins were similar between dominant and subordinate females, it appears the "female protection" from atherosclerosis enjoyed by the dominant monkeys occurred independently of changes in characteristics of plasma lipoproteins.

Although stress reduction and a decrease in coronary artery disease events has been shown in patients who have had a myocardial infarction,[89] the role of behavior modification as a primary intervention tool with respect to disease risk has not been clearly established. Further work is needed to clarify the importance of psychosocial and behavioral effects on the risk for both men and women and to characterize differences in sex responses. In addition, the role of primary intervention in stress reduction or disease risk modification needs to be firmly established.

Pregnancy

Is the most important event in many women's lives a coronary artery disease risk factor? While women are protected during their reproductive years, there is theoretic evidence to suggest that changes in plasma lipid and lipoprotein levels that occur during pregnancy can increase their risk.[90] Plasma levels of total cholesterol and triglycerides increase from prepregnancy levels during gestation. These increased plasma lipids return to prepregnancy levels after gestation. Although plasma HDL-cholesterol levels increase during gestation, they tend to drop below pregestational levels in the postpregnancy state.

Some epidemiologic studies have shown an increased risk of coronary artery disease with parity.[91,92] Others, however, reveal no significant increased risk of coronary artery disease events with the number of pregnancies.[93,94] The Nurses' Health Study, which included 119,963 female participants over a six-year period, found no relationship of myocardial

infarction incidence to an increased number of births or age at first birth when adjusted for risk factors.[95] Further work in this area is important to elucidate the relationship of hormonal events occurring during gestation with their influence on coronary risk factors in women. The application of work of this nature could extend beyond the pregnant condition to provide enlightenment on biologic events related to female protection.

Coronary Artery Bypass Operation and Angioplasty

Invasive therapy exists for both men and women who have shown coronary artery obstruction. Women without evidence of a myocardial infarction who are undergoing a coronary artery bypass operation generally have better left ventricular function compared with men.[96] Operative success, however, is less favorable for women than for men in terms of a higher operative mortality.[96,97] This is likely due to the smaller size of the coronary arteries in women related to less body surface area. In addition, women have other associated medical problems, particularly diabetes mellitus, that render coronary artery bypass procedures more technically difficult.[96] Despite these sex differences in perioperative mortality, postoperative long-term survival is similar in men and women. Similarly, percutaneous transluminal coronary angioplasty procedures are less successful and have a higher mortality in women than in men.[98]

Conclusions

Coronary artery disease represents a major cause of morbidity and mortality in women. Most of the investigation involving its risk factors has involved male subjects. Female subjects need to be the focus of future research, not only because of their risk of heart disease, but also because of unique female risk factors such as oral contraceptive use. In addition, further study is needed to clarify how behavioral and physical activity mechanistically affect the risk of the disease in women.

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There is more difference within the sexes than between them.

IVY COMPTON-BURNETT